

Pediatric Meningoencephalitis Cluster Caused by Snowshoe Hare Virus, Whistler, British Columbia, Canada, 2024

[Announcer] *This program is presented by the Centers for Disease Control and Prevention.*

[Matt Kuehnert] Hello, I'm Dr. Matt Kuehnert, Editor in Chief of the journal *Emerging Infectious Diseases*. EID is an open access, high impact, peer reviewed scientific journal published by CDC. EID publishes articles on new and re-emerging infectious diseases that occur around the world, with the mission of improving the understanding of pathogen emergence, control, and prevention. We are pleased to present selected EID articles to you, brought to life in new and interesting ways through this podcast series.

[Candice Hoffmann] Welcome to the *Emerging Infectious Diseases* podcast. I'm Candice Hoffmann. In the summer of 2024, three children in Canada were admitted to the same hospital, all with meningoencephalitis. Meningoencephalitis is a dangerous inflammation of the brain and its protective membranes. At first, these cases looked like unrelated, unexplained illnesses. But a team of experts pieced together the clues and ultimately traced these cases to snowshoe hare virus, an uncommon mosquito-borne infection. They published their findings in EID. First, we'll hear from two of the authors, Dr. Jennifer Tam and Dr. Faisal Ali.

[Jennifer Tam] Hi, I'm Dr. Jennifer Tam. I work at BC Children's Hospital in Vancouver, Canada as a pediatric infectious diseases physician and I was involved in the cases of the snowshoe hare cluster that we found here.

[Faisal Ali] My name is Dr. Faisal Ali. I'm a pediatric infectious diseases fellow at the University of British Columbia. I primarily work at BC Children's Hospital, and I was involved in this cluster of cases at the start of my infectious diseases fellowship training where I was on a microbiology rotation. So, I was quite heavily involved in the laboratory medicine or diagnostic aspects of the patient's care.

[Candice Hoffmann] Dr. Tam, Dr. Ali, and their colleagues published this article in EID to increase awareness among healthcare and public health professionals of snowshoe hare virus.

[Faisal Ali] It highlights a cluster of children who had meningoencephalitis that went undiagnosed. And eventually we found the cause, which was this emerging virus, the snowshoe hare virus that can be transmitted via mosquito vectors. And it is an important consideration for undiagnosed cases of meningoencephalitis during the summer months and mosquito season in Canada.

[Candice Hoffmann] Alright, so we'll start with the virus. So, what is snowshoe hare virus and why is it called that?

[Jennifer Tam] So, snowshoe hare virus is an arbovirus. So, it's a virus that circulates normally between mosquitoes and small mammals. But humans can accidentally be infected after a mosquito bite. Snowshoe hare virus is part of a larger group of closely related viruses called California serogroup viruses, which includes things like Jamestown Canyon virus, La Crosse virus, and California encephalitis virus as kind of prime examples that are significant in North America. Snowshoe hare virus specifically is found coast to coast in Canada and the Northern U.S. states, so it's quite a wide geographic distribution. And how it got its deceptively cute name

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was that it was first isolated from a snowshoe hare in Montana in the late 1950s. But it does circulate in other small mammals as well, such as rabbits, squirrels, chipmunks, and other rodents. So, when people get snowshoe hare virus, they will have no idea that they got it because it's asymptomatic most of the time. For those who do develop symptoms, it generally happens three to seven days after they get bitten, so that's the incubation period, and it generally presents non-specifically like a typical febrile viral illness. So, one might get fever, chills, nausea, vomiting, headache, abdominal pain, things like that. But a small subset might develop a neuroinvasive disease such as meningitis, encephalitis, or meningoencephalitis. But this is still strikingly rare, which is what makes our cluster of patients quite alarming. But overall, it does seem that snowshoe hare virus is more likely to cause symptoms in kids rather than adults from what we can see in the published literature and what would be in keeping with what we found in our area as well.

[Candice Hoffmann] Arboviruses like snowshoe hare virus are spread by mosquitoes.

[Faisal Ali] The mosquitoes that transmit this virus or the vectors, they're primarily the *Aedes* and the *Culiseta* species of mosquitoes. And those species are pretty widespread and abundant through basically all of Canada, from the Atlantic to the Pacific, as well as the northern states of the United States, so kind of bordering Canada. There's been a lot of studies looking at which particular mosquitoes harbor snowshoe hare virus, and it has actually been isolated in a lot of the field-captured mosquitoes of both the *Aedes* and the *Culiseta* species.

[Candice Hoffmann] How does the virus get from mosquitoes to mammals and humans?

[Faisal Ali] The transmission of snowshoe hare virus through these mosquitoes primarily occurs by two different ways. So, the first is where the mosquito that bites an infected animal, be it a snowshoe hare or a small rodent, picks up the virus and transmits it to the next animal, and that could also be a human through a blood meal.

[Candice Hoffmann] The virus also persists in mosquitoes through something called "transovarial transmission".

[Faisal Ali] So what happens is that the mother mosquito passes the snowshoe hare virus to her offspring through the eggs. As a result of this transovarial transmission, the virus itself can persist in the mosquito populations over the winter months as well, because they don't really need that vertebral host, the snowshoe hare or the squirrel, to persist during those kind of colder months.

[Candice Hoffmann] Because the virus can persist in mosquito eggs over winter, risk can return quickly each spring.

Going back to the three cases described in this article, there were three patients with similar symptoms, hospitalized around the same time. Ultimately these cases were connected, but it wasn't obvious right away.

[Jennifer Tam] So case number one is the older of the three pre-adolescents, and she actually presented more like a meningitis with headache, photophobia, neck stiffness, vomiting. And so, she was treated with a 10-day course of ceftriaxone. Then the second patient, who was maybe the flag that signaled that there was a link here, was a toddler who actually had much more pronounced neurological symptoms, more compatible with encephalitis. So, she presented with seizures and through her hospital stay, she even had some word finding difficulties, some blurry vision, and even some visual hallucinations. And then the last patient presented more non-

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specifically with fevers, vomiting, fatigue, and a slow heart rate. But the key in this case that clued us in to a neurological process was that his cerebrospinal fluid white blood count was elevated. He was also ultimately treated with 10 days of ceftriaxone for culture negative meningitis. So, all these patients were admitted for one and a half weeks on average, so quite a profound amount of time to complete their treatment. They did all fully recover from their symptoms, thankfully though, months later. All three families continue to be really engaged with us for further research to better understand this virus.

[Candice Hoffmann] How did the three cases in this paper come onto your radar, and how did you first realize they might be connected?

[Jennifer Tam] It was a bit serendipitous that we came across this cluster, but we hope that raising awareness about this virus will obviously leave things less to chance in the future. But how it happened in our case was I was just chatting with the mom of case number two—so this was the second patient that chronologically presented to our hospital with these symptoms—and the mom just brought up that, interestingly, one of her neighbor's kids was also in the hospital with a similar issue. And our team had actually just finished making a plan for that neighbor whom we were treating as a culture-negative meningitis because we didn't find anything else on the initial investigations. And for that first patient, when she was just the only one, I remember talking to our infectious diseases division group and asking, you know, at what point should we start thinking about less common causes like the California serogroup viruses? And we didn't totally come to a consensus because we just had that one patient. But then when we had these two patients linked together, we immediately alerted our microbiologists who helped to arrange further testing. And coincidentally, on this same day, we also received a new consult request for the young boy who is our third patient in the case, who we realized was also from the same area presenting with abnormal neurological testing. And so that's what really caught our attention as an epidemiological signal, if there ever was one.

[Candice Hoffmann] With three children from the same area with overlapping hospital stays, with similar neurological symptoms, this was beginning to look like more than a coincidence.

[Jennifer Tam] In our case, without the epidemiological link, to be honest, I'm not sure we would have gone marching that much farther because unfortunately, many of these rare things like snowshoe hare virus don't have actual treatments. And there was nothing obvious that made us suspect mosquito bites up front because they were not covered in mosquito bites, these kids or anything, but it was summer and all the children spent a lot of time outdoors. And so, we knew it was a possibility. And so, when we think about encephalitis cases, California serogroup viruses is on our list of what we would think of next if we wanted to go further.

[Candice Hoffmann] So how did all the specialists in the hospital collaborate to determine the cause of the children's symptoms?

[Faisal Ali] Their care was actually kind of overlapping between different teams within the hospital, so obviously the general pediatrics team, pediatric neurology team, the infectious diseases team. And I think it was an interesting interplay between all of those different kind of subspecialists and trying to piece together the diagnosis because initially when we didn't really have that diagnosis that it's snowshoe hare virus meningoencephalitis, there was a lot of different differentials, be it bacterial meningitis, other viral meningoencephalitis or even autoimmune encephalitis. So, there was a lot of brainstorming and probably problem solving happening

behind the scenes with all of those different subspecialists. And it just goes to show how, you know, these things can develop before you ultimately find your diagnosis.

[Candice Hoffmann] Multiple lab levels were involved in the diagnostic testing that ultimately identified snowshoe hare virus.

[Jennifer Tam] We have our local microbiologists at BC Children's Hospital, but then lot of the testing is actually done through the British Columbia Centre for Disease Control or BC CDC, which is our provincial public health lab. From there, there are some tests that are done actually at a national level.

[Candice Hoffmann] Do tests for snowshoe hare virus go to the national lab in Canada?

[Jennifer Tam] That has to go to the national lab, exactly. And so, that does add to the turnaround time. So as of now, we still send everything to the NML or the National Microbiology Lab.

[Candice Hoffmann] A public health investigation was launched after the first three cases were identified. This investigation uncovered a fourth case of snowshoe hare virus. Another author of this article, Dr. Rohit Vijh, explained how this investigation unfolded.

[Rohit Vijh] My name is Dr. Rohit Vijh. I am a medical health officer at Vancouver Coastal Health Public Health, and I serve as the medical director for communicable disease control for our Vancouver Coastal Health region, which includes the Sea-to-Sky region of Squamish, Whistler and Pemberton. So, when Vancouver Coastal Health was notified of these three pediatric cases in late September 2024 that had occurred amongst residents living within the Whistler region, we immediately recognized that this was unusual. And in particular, when all three children had been hospitalized in August and laboratory testing had identified them with this snowshoe hare virus, we sort of really kind of jumped into action to really understand what was going on here as this was a virus that we had not seen before within this region present this amount of severity and this clustering in time. And so, for the first part of our response, which was supporting the affected families and clinical teams, we worked really closely with our colleagues at BC Children's Hospital, with our public health colleagues at the public health laboratory at the BC Centre for Disease Control and the different infectious disease specialists to better understand the person demographics and the risk factors of our different cases. What was really challenging for us was that Jamestown Canyon, snowshoe hare, and these California serogroup viruses were not reportable in British Columbia to public health at that time, and in fact, what was reportable to us was encephalitis and meningitis, but because of that, we did not have like a standardized case definition, we didn't have a standardized case report form of like questions like we would for other types of communicable diseases such as measles or pertussis.

[Candice Hoffmann] Reportable diseases are illnesses that, by law, must be reported to public health authorities when diagnosed. The list of reportable diseases varies from place to place. Because snowshoe hare virus and related viruses weren't reportable in British Columbia, investigators had to create their own plan. They drew on practices from places where these infections are reportable, creating a working case definition and a short questionnaire to guide what information to collect.

[Rohit Vijh] And so, where we had to start in our investigation was really looking to other jurisdictions within the U.S. and other parts of Canada where it was reportable to really understand how do we classify these cases and also what pieces of information we need to collect to kind of collate together to kind of inform our public health response in caring for these

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cases and also to identify any additional sources to mitigate them. And so, what that required us to do was to kind of put this hodgepodge of different questions into a case report form and give that to our environmental health officers who worked with the different families to collect the different pieces of information and a lot of that information is what you guys see in figure one in the paper of really understanding when their symptoms started, when their exposure period would have occurred, when were they hospitalized, to really see like were these cases actually happening very close in time? And then also connecting with the families to understand where they may have gone, whether they may have traveled outside a province, whether they stayed in different parts of BC to really identify, are there commonalities in these cases of where they could have been exposed? And what we determined through our investigation was that all these individuals had sort of stayed local to the Sea-to-Sky region. They had all been in outdoor settings and had numerous mosquito bites and there were some settings that they had had in common. And that was very useful because I think it really helped us understand that this was an emerging pathogen that was occurring within our region with this level of severity for the first time in the documented history in British Columbia. And that those mapping and these exercises were really kind of integral to some of the mosquito surveillance that has been set up in the past two years within the region.

The other part or the last part of our response after kind of identifying these exposures was really around identifying any other potential infections that may not have been reported to us or may not have been tested for this virus because it's not very common in the differential for encephalitis and meningitis at the outset. And so, what we did is we kind of issued this targeted physicians and nurse practitioner update within the region to report any cases of unexplained neurological illness, any cases of encephalitis and meningitis that did not have an identified pathogen that had occurred within the season in 2024, so that we could potentially connect with them and arrange for additional testing to see if potentially these clinical presentations were associated with California serogroup virus. The alert to community physicians is actually a regular tool that we use in public health for either novel infectious diseases or re-emerging infectious diseases. And they're really meant to sort of help raise awareness to physicians as to what's kind of going on locally in their area to help them either, you know, look at patients that are coming in and ask the right questions or kind of keep a certain infectious disease a bit higher on their differential than they might normally because it is circulating. And so, we do this quite regularly for other types of diseases like measles and pertussis, for example. But in this case, we really wanted to put out this alert because this was something very novel. It's not something that is often tested for. And in these alerts, we sort of talk about like signs and symptoms they should look for, the type of testing they should order. And as a result of that, we did have a physician reach out to us who had a patient, an adult patient this time, who had had encephalitis with no infectious cause and had subsequently been treated for autoimmune encephalitis with immunocompromising medication. And we were able to kind of get some bank specimens, collect additional specimens, and were able to actually confirm that this individual actually had likely California serogroup virus that had explained their encephalitis picture, and as a result had sort of been taken off these medications that were suppressing their immune system that were no longer needed, and the person subsequently recovered.

[Candice Hoffmann] In addition to the public health investigation that Dr. Vijn described, there was a mosquito surveillance pilot to find out which species are in the region and what viruses they might be carrying. Leading that work was Dr. Anya Smith from the BC Centre for Disease Control.

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[Anya Smith] Hello, my name is Dr. Anya Smith. I'm a senior scientist with the British Columbia Centre for Disease Control in Vancouver, Canada. I'm also a clinical associate professor within the School of Population and Public Health at the University of British Columbia, also in Vancouver. So, I lead applied research and targeted surveillance involving zoonotic and vectorborne diseases, and have a background in epidemiology and public health, and I've been at the BC Centre for Disease Control for over two and a half years.

[Candice Hoffmann] Dr. Smith led the Sea-to-Sky surveillance project. She starts with where and when it launched.

[Anya Smith] So, to set the study area for those individuals listening who don't know the Sea-to-Sky, it's about a 130-kilometer stretch of highway along the southwest coast of British Columbia. It's a very beautiful stretch of highway, very scenic, and has multiple municipalities along it including Pemberton and Whistler, which many people probably have heard of, and Squamish. And so, together with multiple partners last year in the summer of 2025, we launched a mosquito surveillance study. And I should just mention that our partners included Vancouver Coastal Health, which is the health authority overseeing that region, also the Department of Zoology at University of BC, also Lilwat First Nation, Squamish First Nation, and also, I should mention thanks to funding from University of British Columbia Centre for Disease Control. So, all of us together launched this study in response to a cluster of four encephalitis cases that occurred in the region in the summer of 2024.

So last year, we wanted to go in and get a sense of what endemic and invasive mosquito species were circulating in the area and also what viruses they may be carrying, if any, and namely California serogroup viruses and West Nile virus. So, we also wanted to inform the current risk to public health by doing this study as well. So, we set up multiple mosquito traps, I believe 11 mosquito traps, along the corridor from Pemberton through Whistler and Squamish to trap mosquitoes. And then these mosquitoes were taken back to the Department of Zoology at UBC and identified to the species level and then sent to the public health lab at the BC CDC for pathogen testing.

[Candice Hoffmann] Next, Dr. Smith described how the researchers chose mosquito collection sites and how they collected mosquitoes.

[Anya Smith] So the way we choose sites, once we have that geographic area, we use satellite view on Google Maps to really get a sense of certain features, so things like where the forested areas are, you know, where mosquitoes like to hang out. We also look for where stagnant water is, so you know, they love to breed in stagnant water. We look for industrial areas because some species of mosquitoes really are urban dwelling and prefer those areas. We also look for features like parks, schools, trails, recreational areas where people could potentially be exposed. We also look for First Nations communities if we are partnering with First Nations and if, of course, we have permission to access those communities. So, we look for all of these features first. We also contact our municipal and city partners and ask, you know, has the public sort of raised concern about an uptick in mosquito activity in certain areas? And so, we use all of this information to kind of get a preliminary list of potential sites. Then what we do is we do a recon day, as we call it. So, we go and we actually hit the ground, and we take a look at all these sites in person. And we look more closely at things like how sheltered from the extreme elements is it? So, you know, if it's too windy, they're going to blow around, we're not going to catch them. If they're exposed to extreme heat, they'll desiccate. You know, they like the warm temperatures,

but if it's extreme and very exposed, then that's not good either. We also look for where we could hang or set traps where trap disturbance is minimal. So, believe it or not, people do come in and vandalize or steal traps. I don't know why, but it happens. And so, you know, we kind of...we consider all of these things, and we also of course consider accessibility. We don't want one of our students to be going and having to hike half an hour into a site either. You know, we have so many hours in the day. So, all of those things play in. And so that's how we kind of choose the sites, and then we narrow those down and then we have our final set of sites.

In terms of how we collect them, we have multiple different types of traps, and those are largely due to either this, you know, they lure certain species of mosquitoes or genera of mosquitoes, also mosquitoes that are in certain physical states. So, for example, one of the ones that we use is called the CDC light trap. And it's a very general trap. It catches multiple different species of mosquitoes, and it uses light and carbon dioxide as a lure for those mosquitoes, they're usually hung, so hung from a branch about a meter to a meter and a half off the ground, and like I said, a wide range of mosquito genera like *Aedes*, *Anopheles*, and *Culex* species, which are which are around the area. We also have what we what's called a BG-Pro Sentinel trap. This trap is typically set on the ground and it's really targeting species within the *Aedes* genera. And so *Aedes*, a lot of them are urban adapted and so they do like industrial sites and laying eggs in old empty tires with water that's accumulated. They're container breeders essentially. And so, we set those closer to the ground where they're flying and hoping to catch more of them. And again, they use carbon dioxide as a lure for those mosquitoes. And then thirdly, we also have what are called gravid traps. And so those are interesting. They're trying to lure female mosquitoes that have had a blood meal and are ready to lay their eggs. And so, what we use as a lure is what we call a hay-brewed tea. It's supposed to smell like and mimic stagnant water for them to come and lay. And so, those are used to specifically lure these blood-fed females. And so, with those three in mind, we set those across the different sites, and we have students that come on a set morning of every week to set up the traps. And then 24 hours later, the student comes back around the same time to collect the mosquitoes and bring them back to UBC. And so, what we want is to allow for that 24-hour period to include the dusk-to-dawn period where a lot of mosquitoes are active. And so that's the summary of what we do.

[Candice Hoffmann] So what's next? With early findings in hand, the team has expanded the work to a nearby, more populated region.

[Anya Smith] Yeah, so the study...so we have expanded to the North Shore, which is a region that's adjacent to the Sea-to-Sky corridor. And so, we are expanding the work that we did in the Sea-to-Sky to the North Shore for a couple of reasons, one of which is although we just found two positive pools in the Sea-to-Sky, we did find the virus in mosquitoes in that area. And we also know that the North Shore is a more populated area, a much more populated area. So, you've got larger populations that are living within or near prime mosquito habitat. And so, we really want to expand the work out. And so, what that means is we want to have a primary data set where we can look back in the future when doing similar work to understand what the trends might be in the distribution of invasive and endemic mosquito species and the viruses that they're carrying, if any.

[Candice Hoffmann] So, the aim now is to build a baseline data set, tracking mosquito species and any viruses they may carry, so public health officials can spot trends and respond sooner. This work relies on strong partnerships across public health, academia, First Nations, and municipalities. Dr. Smith names several.

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[Anya Smith] Again, in partnership with Vancouver Coastal Health, Department of Zoology at UBC, we're partnering with Squamish Nation, once again, also Tsleil-Waututh Nation, First Nation, and also municipal and city partners in North and West Vancouver. Also, it's funded by the Lionsgate Hospital Foundation, UBC CDC, and the UBC Faculty of Medicine.

[Candice Hoffmann] While researchers work to learn more about how snowshoe hare virus spreads among animals and mosquitoes, there's information that healthcare and public health professionals can act on now.

[Rohit Vijh] So for clinicians, I think what's really important is within our region, we've had multiple rounds with infectious disease and medical microbiologists to really kind of consider California serogroup viruses in patients that are presenting with unexplained meningitis and encephalitis during the mosquito season, particularly if they've had exposures within these parts of our province. And that really early consultation with public health and our public health lab colleagues is really important so that the appropriate testing can be organized and expedited to help establish that diagnosis, and that even though these infections are uncommon, they still may be an unrecognized cause of neurological illness in some communities. And so, it's always important to kind of consider it as part of your differential for these meningitis and encephalitis when other more common viral causes have been ruled out.

[Candice Hoffmann] What advice do you have for families and children to protect themselves from snowshoe hare virus and other arboviruses?

[Rohit Vijh] Families can reduce their risk by using insect repellent approved for children and following those label directions, wearing long sleeves and pants when mosquitoes are most active, potentially avoiding or being more cognizant during dusk and dawn periods when mosquito activity is greater, using things like window screens at night to kind of reduce the amount of mosquitoes that might be coming in and avoiding sort of areas with heavy mosquito activity. And other things that people can also do is really be cognizant of reducing standing water near your home, clear or drain anything that can hold stagnant water, like plant pots, so that the mosquito larvae don't have time to breed in those areas. And so, I would say really what they can do to protect themselves are all the things that we recommend around kind of preventing getting mosquito bites to begin with. I also think it's important to put risk into perspective. Most of these infections are thought to be asymptomatic or cause very mild illness and that severe, neurological disease is quite uncommon. But you know, families that might be in these areas and their child sort of develop more severe neurological symptoms should promptly seek medical attention.

[Faisal Ali] At the end of the day, in terms of advice, for practical advice for families with children, is that mosquito bites are mostly an annoyance, but in some cases they can transmit these viruses that can sometimes cause severe and serious illness. And so, I think it's important to make sure that we try our best to prevent mosquito bites and reduce their areas of breeding. But at the end of the day, kids should still be able to enjoy the outdoors in the summer for sure and go out and play in their backyards and parks.

[Candice Hoffmann] Thanks for listening to our podcast. We hope you'll become a regular reader of EID, where you can find articles like this one.

[Rohit Vijh] I definitely do regularly read EID. I think it's a journal that as a public health physician who works in communicable disease control is really a source where I have often

found different outbreak investigations being reported or different disease topics that are being discussed, and it often is a really rich resource for me as part of my own professional learning and continuing medical education to really stay up to date with what's current or novel within my field to help inform my own practice and clinical decision making.

[Jennifer Tam] We chose to publish in EID because we know it's a far reaching, high-impact journal. And we did feel that this cluster was quite intriguing and would be of interest to broader audiences than just pediatric infectious diseases, for example.

[Candice Hoffmann] You can read the full article, "Pediatric Meningoencephalitis Cluster Caused by Snowshoe Hare Virus, Whistler, British Columbia, Canada, 2024".

[Outro] The conclusions, findings, and opinions expressed by authors contributing to this journal do not necessarily reflect the official position of the U.S. Department of Health and Human Services, the Public Health Service, the Centers for Disease Control and Prevention, or the authors' affiliated institutions.

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